Cell Stem Cell
Forum

Assessing State Stem Cell Programs in the United States: How Has State Funding Affected Publication Trends?

Hillary B. Alberta,[1] Albert Cheng,[2,4] Emily L. Jackson,[3] Matthew Pjecha,[1] and Aaron D. Levine[1,4,*]
[1]School of Public Policy
[2]George W. Woodruff School of Mechanical Engineering
[3]School of Chemical and Biomolecular Engineering
[4]Petit Institute for Bioengineering & Bioscience
Georgia Institute of Technology, Atlanta, GA 30332, USA
*Correspondence: aaron.levine@pubpolicy.gatech.edu
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Several states responded to federal funding limitations placed on human embryonic stem cell research and the potential of the field by creating state stem cell funding programs, yet little is known about the impact of these programs. Here we examine how state programs have affected publication trends in four states.

INTRODUCTION

The isolation of human embryonic stem cells (hESCs) in 1998 intensified discussions about ethical issues associated with stem cell research and inspired a still-ongoing global policy debate over the acceptability of and funding for various types of stem cell research (Gottweis, 2010). In the U.S., three distinct federal funding policies—corresponding to the Clinton, Bush, and Obama Administrations—have been adopted (Gottweis, 2010), and the policy environment has been further complicated by uncertainty associated with congressional action and litigation (Levine, 2011).

Extensive policy action has also occurred at the state level in the U.S., with states both supporting and restricting stem cell research and related areas of scientific inquiry (Levine et al., 2013). Six states—California, Connecticut, Illinois, Maryland, New Jersey, and New York—took the unusual step of dedicating state funding to support basic and translational stem cell research (including research using hESCs) (Karmali et al., 2010). These state policies had several goals encompassing the advancement of science (including hESC research that could not be conducted with federal funding during the Bush Administration) and economic development priorities. Although stem cell funding programs in Illinois and New Jersey have ceased operations, funding programs of various sizes—ranging up to California's $3 billion program—continue in the other four states (see Table 1 for details on these programs and information on their size relative to NIH funding in each state).

Despite the scale of these programs, relatively little is known about their impact on the field. One exception is a 2010 assessment that found that between December 2005 and the end of 2009, the programs collectively awarded nearly 750 grants totaling approximately $1.25 billion in state funding (Karmali et al., 2010). This assessment found wide variation (ranging from 21% in New York and New Jersey to 97% in Connecticut) among the states in the extent to which their grants focused on hESC research and suggested that one key success of the programs had been drawing new scientists into the field of stem cell research (Karmali et al., 2010).

As some of these state programs are nearing the final years of their initial funding commitments, understanding their effects on the scientific enterprise is an increasingly important policy question. Here, we contribute to this effort by examining publications in stem-cell-related fields in the four states with sustained stem cell funding programs and comparing the share of hESC- and induced pluripotent stem cell (iPSC)-related publications with the share of publications in other areas of biomedical research (RNAi- and cancer-related research), which were presumed to be less affected by state policies. In addition, we examine the funding sources acknowledged in both hESC- and RNAi-related publications to assess how state funding contributed to the differences we observe. Our analysis builds on previous efforts that have looked at the international distribution of stem cell publications generally (Guhr et al., 2006; Levine, 2004, 2008) and the publication performance of the United States following the adoption of the restrictive funding policy in the Bush Administration more specifically (Furman et al., 2012; Owen-Smith and McCormick, 2006). (See Supplemental Information for more details about our analysis strategies.)

Publications Trends Vary by State

We first looked at the share of U.S. hESC-, iPSC-, RNAi-, and cancer-related publications with at least one author from California, Connecticut, Maryland, or New York as well as the share of hESC-related publications acknowledging funding from each state (see Figure 1). We also grouped the publications based on when they were published in relation to the various policies that have been enacted. The difference between each state's share of hESC- and iPSC- related publications and its share of cancer-related publications was calculated for three timeframes (Table S1), which represent (1) the period when hESCs were under investigation but state policies had not yet been adopted (early hESC: 1998–2004), (2) the period during which most state stem cell funding policies were adopted and awarded their initial grants (adoption: 2005–2008), and (3) the period when these programs were up and running (implementation: 2009–2013). Given time lags between funding

Table 1. Overview of Four Major State Stem Cell Research Funding Programs

	California	Connecticut	Maryland	New York
First grants awarded	2006	2006	2007	2008
Initial funding/Time period	$3B/10 years	$100M/10 years	N/A	$600M/11 years
Approximate annual funding	$300M	$10M	$14M	$55M
NIH Funding (FY13)				
hESC	$36M (28.8%)	$4.4M (3.5%)	$2.4M (2.0%)	$7.9M (6.4%)
SC	$222M (20.3%)	$21M (1.9%)	$41M (3.8%)	$108M (9.8%)
All	$3.3B (14.8%)	$445M (2.0%)	$1.6B (7.1%)	$1.9B (8.6%)

Notes: Approximate annual funding was calculated by dividing total commitment by time period of commitment for California, Connecticut, and New York. Maryland's approximate annual funding was calculated by dividing its total funding through July 2014 by its years of operation. For comparison, NIH funding received by each state for hESC, all stem cell (SC) and all extramural research is shown for fiscal year 2013. The total dollar value of NIH funding was extracted from the NIH RePORT system (http://report.nih.gov/), and the share of all NIH extramural funding in that category was calculated from these data.

and publication, we assumed that their effects would most likely be seen in the publication record during this final period.

California's share of publications in the two comparison groups (RNAi- and cancer-related research) was quite consistent. Between 15% and 18% of U.S. cancer-related publications had at least one author from the state in each 2-year period assessed between 1996 and 2013, and following an initial period of growth, the state's share of RNAi-related publications remained between 17% and 19% from 2002 through 2013. The state's share of hESC- and iPSC-related research differed markedly from its share of these comparison groups. Its share of hESC-related research exceeded its share of the comparison groups as early as 2000 to 2001, and this difference continued to grow in future years, with the state's share reaching 45% in 2010 to 2011. California's share of iPSC-related research has been high since shortly after the technology's discovery, with the state accounting for 44% of U.S. publications in 2008 to 2009. These differences are statistically significant in both the adoption and implementation time periods for hESC-related research and during the implementation period for iPSC-related research (see Table S1). After the California Institute for Regenerative Medicine (CIRM) issued its first grants in April 2006, the share of articles acknowledging California funding increased rapidly from approximately 3% in 2006 to 2007 to more than 20% in 2010 to 2011 and 2012 to 2013. Overall, California state funding was acknowledged in nearly 19% of all hESC-related articles in our data set published between 2006 and 2013, compared with 1.8% of articles in a comparable set of RNAi-related research (t test, $p < 0.01$). 45% of the hESC-related articles published between 2006 and 2013 in our data set with at least one author from California acknowledged funding from the state.

Similar trends were seen in Connecticut. The state's share of cancer-related publications was relatively consistent, ranging from 2% to 3% throughout the time period studied, while the state's share of hESC-related research grew from 0% in 2002 to 2003 to 6% in 2012 to 2013. Similar to California, Connecticut's share of iPSC-related research publications exceeded its share of cancer-related research as early as 2008 to 2009, and in Connecticut's case, this difference continued to grow through 2012 to 2013. These differences are statistically significant in the implementation time periods for both hESC- and iPSC-related research (see Table S1). Overall, Connecticut state funding was acknowledged in 2.4% of all hESC-related articles published between 2006 and 2013 in our data set, compared with 0.2% of articles in the comparable set of RNAi-related research (t test, $p < 0.01$). 67% of the hESC-related articles published between 2006 and 2013 in our data set with at least one author from Connecticut acknowledged funding from the state.

For Maryland and New York, in contrast, the share of hESC- and iPSC-related research in recent years was similar to the share of the two comparison groups. Maryland's share of hESC-related research declined from a high of 22% in 2004 to 2005 to 10% in 2008 to 2009 before leveling off. State funding from Maryland was acknowledged in 2.2% of the hESC-related articles published between 2006 and 2013 in our data set, with most of these state-supported articles published between 2010 and 2013. In New York, the share of hESC-related research publications grew from a low of 8% in 2008 to 2009 to 13% in 2012 to 2013 but, even following this growth, remained similar to the state's share of publications in the two comparison groups. Funding from New York was also acknowledged in 2.2% of the hESC-related articles published between 2006 and 2013 in our data set, and most of these articles were published between 2010 and 2013.

Policy Considerations

Our comparative analysis provides some of the first evidence that the distribution of stem-cell-related publications in the United States differs from the distribution of publications in fields not targeted by specific state funding policies, and our analysis of the funding sources acknowledged in many of these articles strongly suggests that state funding is responsible, in part, for these differences. The share of hESC- and iPSC-related publications produced in each of the four states examined depends on a variety of considerations, including the size, strengths, and interests of the scientific community and the specifics of the policy itself (i.e., its timing, its size, and its focus). In addition, it depends on the competitive environment within the United States, as over-performance in one state must be balanced by under-performance in others.

In both California and Connecticut, state funding programs appear to have contributed to over-performance in the field. In California's case, the state was already a strong performer in hESC-related research before its state funding policy was adopted in 2004, and funding began flowing in 2006. This may reflect a generally supportive state environment or a first-mover advantage, as Geron Corporation, a key funder of early hESC research, is based in the state. Following passage of Proposition 71 in November 2004 and the creation of CIRM in the ensuing years, the state's share of hESC-related research grew from

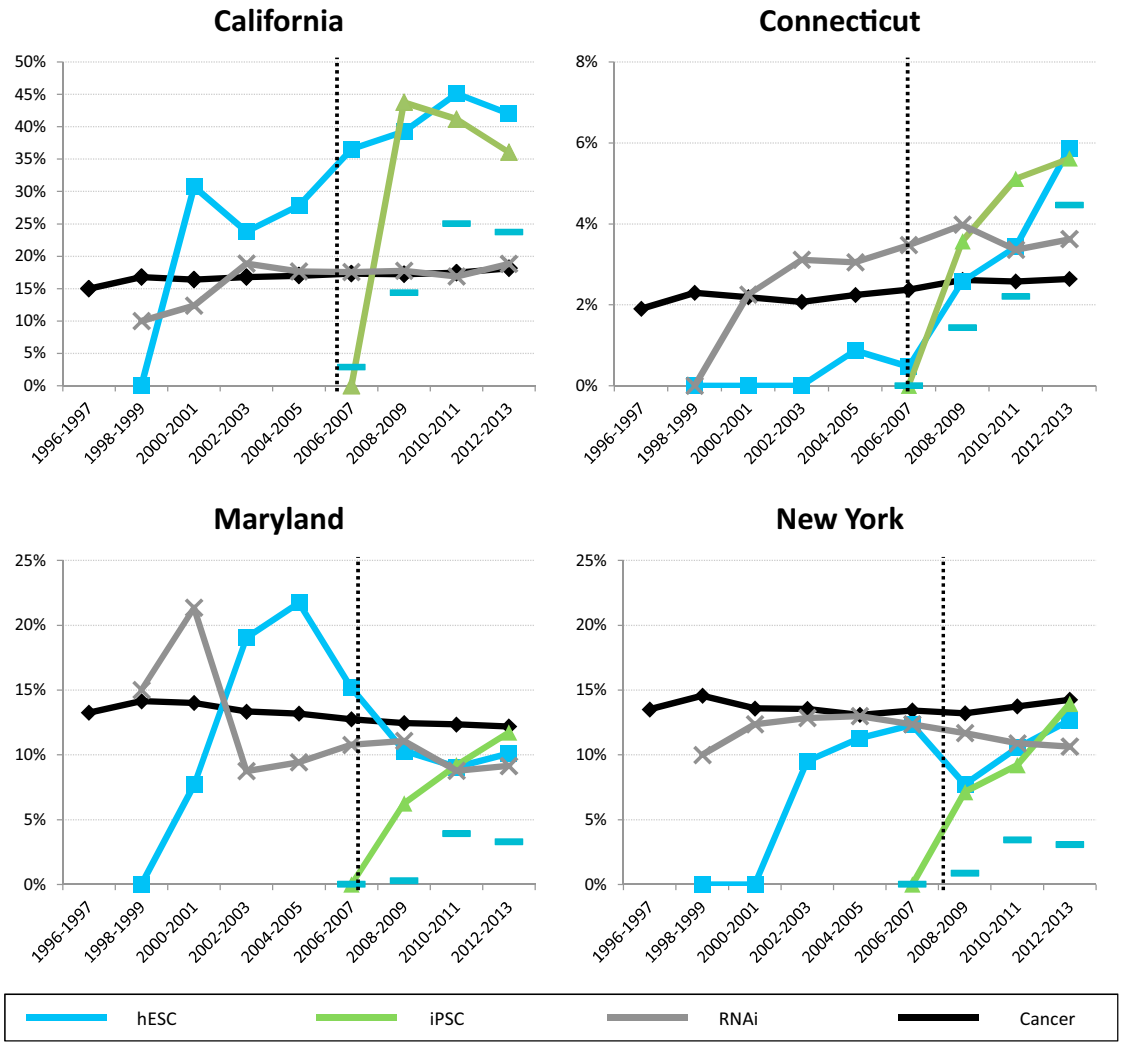

Figure 1. Trends in State Publication Percentages for hESC-, iPSC-, RNAi-, and Cancer-Related Research
Note: Each panel shows the percentage of U.S. publications in the four fields with at least one author from the specified state (solid lines) and the percentage of hESC-related research publications that acknowledged funding from the specified state (blue dashes). Vertical bars indicate the approximate time at which each state stem cell program awarded its first grants. See also Table S1.

approximately 25% in 2002 to 2003 to more than 40%, and the state maintained this position of strength in both hESC- and iPSC-related research from 2008 through the end of our data in 2013. Between 2010 and 2013, approximately 55% of hESC-related articles published with at least one California author acknowledged state funding, suggesting that this funding program played an important role as California maintained and built upon its early leadership in the field. The Connecticut case is even more suggestive of a policy impact, as the state showed very little hESC-related research activity through 2004 to 2005 and then showed steady growth in publication share following adoption of its funding policy in 2005, with approximately 67% of these articles acknowledging state funding. These findings align well with previous work (Karmali et al., 2010) indicating that California and Connecticut, at least in the early years of their funding programs, focused more of their grants on hESC research than did other states. Given the close relationship between hESC and iPSC research (Scott et al., 2011), it is not surprising that, although iPSC cells were not explicitly prioritized by these state programs, these states also produced a higher share of iPSC-related research than they did in the comparison fields.

In contrast to California and Connecticut, over-performance in pluripotent stem cell research was not seen in Maryland and New York. Our analysis shows, however, that state funding from each of these states contributed to approximately 3% of the hESC-related publications in our data set between 2010 and 2013. This funding appears to have helped these states maintain a share of hESC-related research similar to their share in the comparison fields, and given the competitive environment with other states investing heavily in stem cell research, this may well be a successful policy outcome.

This analysis illustrating the relative performance of states in the production of stem-cell-related research publications provides a useful starting point for policymakers and, potentially, voters considering

the future of state stem cell funding efforts as well as others interested in state science and technology policy more generally. We focused our analysis on hESC-related research as this field was a key motivation for some state stem cell funding programs (Karmali et al., 2010), but future work could examine the effects of state stem cell programs on the broader fields of stem cell research and regenerative medicine. In addition, while we analyzed hESC-and iPSC-related research separately, these fields are closely intertwined (Scott et al., 2011) (see Supplemental Information for discussion), and future work could examine how state programs reacted to the development of iPSCs and prioritized their funding among these two related but distinct forms of pluripotent stem cell research. In addition, publications are only one measure of the impact of state science funding programs, and examining other outcomes (e.g., patents awarded, clinical trials initiated, etc.) is an important topic for future investigation. Indeed, more thorough efforts to evaluate these state stem cell programs, ideally drawing on the initial goals of the programs and a wide range of relevant outcomes, would be an important step to help assess their impact on the field and the value of field-specific state science funding programs more generally.

SUPPLEMENTAL INFORMATION

Supplemental Information includes one table and Supplemental Experimental Procedures and can be found with this article online at http://dx.doi.org/10.1016/j.stem.2015.01.007.

AUTHOR CONTRIBUTIONS

H.B.A., A.C., E.L.J., and M.P. collected data, designed and conducted initial analyses, and wrote an initial draft of the manuscript. A.D.L. collected additional data, revised the analyses, and prepared the final manuscript. All authors approved the final version of the manuscript.

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